

AMENDMENTS TO THE SPECIFICATION

In the specification, please replace the paragraph beginning at line 3 on page 26 with the following paragraph:

Figures 10A-D illustrate nanoelectrodes that are coupled to microfluidic devices. Figures 10A and 10B show top and side views, respectively, of a microfluidic chip having a "spokes wheel" design. As can be seen in Figure 10A, the chip comprises a substrate with a plurality of microfluidic channels 8 whose inlets are radially disposed about the circumference of a measurement chamber 7 which contains a nanoelectrode 1-impaled or nanoelectrode 1-contacted cell 6. Solution through the channels can be regulated (e.g., by pressure and/or voltage differentials) to provide for sequential delivery of drug candidates into the measurement chamber. In order to register the action of the drug candidates on the cell, a nanoelectrode is inserted into the cell to measure changes in its electrical properties. Figure 10B shows an enlarged view of the measurement chamber 7 and the insertion of a nanoelectrode 1 into the cell 6 as it is exposed to solution flow from a microchannel 8 L7. Substrate (205) is shown. Figures 10C-D show top and side views, respectively of a chip-based nanoelectrode having a similar spokes wheel design. In this embodiment, the nanoelectrode is part of the chip itself (see, Figure 10D).

In the specification, please replace the paragraph beginning at line 17 on page 26 with the following paragraph:

Figures 11A-D illustrate a system for scanning a cell impaled with a nanoelectrode across multiple collimated streams containing drug candidates. As shown in Figure 11A, substrate 305 comprising a plurality of channels 8 which feed into a cell chamber is placed in proximity to nanoelectrode 1 and holding pipette 9. Proper positioning of a cell by holding pipette 9 and/or insertion of nanoelectrode 1 into cell 6 can be visualized by making the cell chamber at least partially optically transparent so that light absorbed and/or transmitted by the cell can be measured. Nanoelectrode 1 is used to measure the electrical properties of cell 6 as it is scanned across microchannel inlets that open into the cell chamber (see, e.g., as show in Figures 11B-D).

In the specification, please replace the paragraph beginning at line 6 on page 27 with the following paragraph:

Figure 13 is a perspective view of a kit in accordance with one aspect of the invention illustrating a process for dispensing fluids from 96-well plates onto a microfluidic chip substrate 405 comprising interdigitating reservoirs using automated array pipettors and cell delivery using a pipette.

In the specification, please replace the paragraph beginning at line 10 on page 27 with the following paragraph:

Figures 14A-C comprise a top view of a microfluidic chip structure for HTS of drugs according to one aspect of the invention, for scanning a sensor such as a nanoelectrode-impaled cell or cells across interdigitated ligand and buffer streams. Figure 14A depicts the overall chip substrate 405 structure for both a 2D and 3D microfluidic system. Figure 14B shows an enlarged view of the reservoirs of the chip and their individual connecting channels 8. Figure 14C shows an enlarged view of interdigitating microchannel whose outlets intersect with the measurement chamber of the chip.

In the specification, please replace the paragraph beginning at line 4 on page 28 with the following paragraph:

Figures 17A-N are schematics showing chip designs for carrying out cell scanning across ligand streams using buffer superfusion to provide a periodically resensitized sensor. Figure 17A is a perspective view of the overall chip design and microfluidic system. Nanoelectrode 1 is shown. Figures 17B-G show enlarged views of the outlets of microchannels and their positions with respect to a superfusion capillary and a nanoelectrode-contacted cell, as well as a procedure for carrying out cell superfusion while scanning a nanoelectrode-contacted

cell across different fluid streams. "P" indicates a source of pressure on fluid in a microchannel or capillary. Bold arrows indicate direction of movement. Substrate 505 is shown. Figures 17H-17N show a different embodiment for superfusing cells. As shown in the perspective view in FIG. 17H, instead of providing capillaries for delivering buffer, a number of small microchannels placed at each of the outlets of the ligand delivery channels are used for buffer delivery. As nanoelectrode 1-contacted cell 6 is moved to a ligand channel and the system detects a response, a pulse of buffer can be delivered via the small microchannels onto the cell for superfusion. The advantage to using this system is that varying the delay time between signal detection and buffer superfusion can precisely control the exposure time of the nanoelectrode-contacted cell to a ligand. Figure 17I is a cross-section through the side of a microfluidic system used in this way showing proximity of a nanoelectrode-contacted cell to both ligand and buffer outlets. Figure 17J is a cross section, front view of the system, showing flow of buffer streams. Figure 17K is a cross-section through a top view of the device showing flow of ligand streams and placement of the buffer microchannels. Figures 1-7M show use of pressure applied to a ligand and/or buffer channel to expose a nanoelectrode-contacted cell to ligand and then buffer.